UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,273	10/15/2001	Chrisotpher John Robert Thomas	13101/48801	4447

7590 09/22/2004

Anthony Giaccio, Esq.
KENYON & KENYON
One Broadway
lNew York, NY 10004

EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,273	THOMAS ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *2,4-6,8,9,18-20,24,25 and 27-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,10-17,21-23 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *28-37* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed June 23, 2004 has been entered.

Claims 1, 3, 7, 10, 11, 12, 13, 14, 16, 17, 21, 22, 23 and 26 are currently amended.

Claims 28-37 are newly added.

Claims 1-37 are pending.

Claims 2, 4-6, 8-9, 18-20, 24-25 and 27 were withdrawn from consideration in the office action mailed December 24, 2003.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Election/Restrictions

Newly submitted claims 28-37 are directed to an invention that is independent or distinct from the invention originally elected for the following reasons: the originally elected invention is directed to the use of a chimaeric gene comprising a promoter which is induced at, and or adjacent to, a target site, wherein expression of the chimaeric gene causes plant cytotoxicity at a target site, whereas the newly submitted claims are directed to the use of a chimaeric gene comprising a tissue specific inducible promoter wherein the chimaeric gene is expressed in and/or adjacent to a target tissue after induction, including uses wherein expression of the chimaeric gene inactivates ribosomes in and/or adjacent to the target tissue of a solanaceous plant, and further including uses wherein expression of the chimaeric gene confers nematode resistance or pollen sterility in a solanaceous plant. The search and examination required for the

newly claimed chimaeric genes and their uses is not coextensive with the search and examination that was performed for the originally elected invention. Accordingly, claims 28-37 are withdrawn from consideration as being directed to a non-elected invention.

Claim Rejections - 35 USC § 112

Claims 7 and 10-13 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed December 24, 2003.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

Applicant traverses this rejection given that a person of skill in the art at the time this application was filed would have understood the functional definition of "homology" to be a percent similarity with an identified sequence after hybridizing under high stringency conditions with complement of the identified sequence wherein the homologue has catalytic activity. Applicant points out that, given this understanding, claims 10-13 have been amended to define a homologous coding sequence having a percent homology along with hybridization conditions, and a described functionality corresponding to the maize type 3 ribosome inactivating protein, which protein is fully described in the specification as having a certain enzymatic functionality. (reply page 13)

The rejection is maintained with respect to claims 7 and 10-13 because the genus of sequences recited in the claims is not described. Applicant has described only a single sequence that codes for a maize type 3 ribosome inactivating protein (SEQ ID NO:2) and its parts (the α domain and the β domain, separated by a central peptide spacer and flanked by N and C terminal peptides). Applicant has not described other sequences that code for a maize type 3 ribosome inactivating protein, or their parts. Applicant has not described a representative number of sequences that are homologous to SEQ ID NO:2 and that encode polypeptides that retain the activity of a maize type 3 ribosome inactivating protein. Applicant also has not described the structural features of SEQ ID NO:2 that would be retained by homologous sequences that encode polypeptides that retain the activity of a maize type 3 ribosome inactivating protein. Absent a description of a representative number of functional species or the structural features of functional species, the genus of sequences recited in the claims is not described.

Claims 1, 3, 7, 10-17, 21-23 and 26 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a transgenic Solanaceous plant transformed with a chimaeric gene comprising a coding sequence of SEQ ID NO:2 encoding a recombinant mature maize ribosome inactivating protein comprising an α domain and a β domain arranged contiguously, the expression of which inactivates the plant's ribosomes, does not reasonably provide enablement for a method of producing a transgenic Solanaceous plant transformed with a chimaeric gene comprising a coding sequence having 70-90% homology to SEQ ID NO:2 or encoding any unspecified part of a maize type 3 ribosome inactivating protein, the expression of which causes any unidentified type of plant cytotoxicity at

any unspecified target site. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed December 24, 2003.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

Applicant argues that the amendment of the claims to define the homologous coding sequence as having a percent homology along with hybridization conditions and as having a functionality corresponding to the maize type 3 ribosome inactivating protein addresses the concerns raised by the Examiner with respect to the enablement of the sequences recited in the claims (reply pages 13-14).

The rejection is maintained because the amendment of the claims to define the homologous coding sequence as having a percent homology along with hybridization conditions and as having a functionality corresponding to the maize type 3 ribosome inactivating protein does not address all of the concerns raised by the Examiner with respect to the enablement of the claimed invention.

Specifically, the amendment of the claims does not overcome the rejection because the specification does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because the ability of a chimaeric gene comprising a coding sequence of SEQ ID NO:2 to produce plant cytotoxic effects other than ribosome inactivation upon expression is unpredictable. In the instant case Applicant has not provided guidance concerning which cytotoxic effects other than ribosome

inactivation to screen for, as only methods for determining the effect of expressing SEQ ID NO:2 on ribosome inactivation are disclosed. The amendment of the claims to define the homologous coding sequence as having a percent homology along with hybridization conditions and as having a functionality corresponding to the maize type 3 ribosome inactivating protein does not address this concern, as the concern would apply to any maize type 3 ribosome inactivating protein.

The amendment of the claims also does not overcome the rejection because the specification does not enable methods of producing transgenic plants transformed with chimaeric genes further comprising transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or nucleotide sequences operable to facilitate the transformation process and stable expression of the chimaeric gene, as the specification provides no guidance with respect to which specific additional sequences to use or in what combination. In the absence of further guidance, undue experimentation would be required by one skilled in the art to select from among the numerous diverse sequences available those particular sequences that, when included as part of a chimaeric gene encoding a maize ribosome inactivating protein, would function in concert with the chimaeric gene to cause plant cytotoxicity at a target site in the same manner as the chimaeric gene exemplified. The amendment of the claims to define the homologous coding sequence as having a percent homology along with hybridization conditions and as having a functionality corresponding to the maize type 3 ribosome inactivating protein does not address this concern, as the concern would apply to any maize type 3 ribosome inactivating protein.

Claims 1, 21, 22, 23 and 26, and claims dependent thereon, remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "target site", for the reasons of record set forth in the office action mailed December 24, 2003.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

Applicant argues that it is clear from the specification that the "target site" as claimed refers to a location in a plant body. Applicants points out that many examples are provided throughout the specification, and points in particular to paragraphs [0012], [0033], and [0037] - [0040]. (reply pages 15-16).

The rejection is maintained because the examples set forth in the specification do not limit the use of "target site" in the rejected claims. The use of tentative language "for example", "may be", might be" in paragraphs [0012], [0033], and [0037] - [0040] does not define the scope of sites that could be targets, or what they are targets for.

Claims 1, 21, 22, 23 and 26, and claims dependent thereon, remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "which promoter is induced at and/or adjacent to a target site", for the reasons of record set forth in the office action mailed December 24, 2003.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

Applicant argues that their clarification of the meaning of the phrase "target site" addresses the Examiner's concerns about the phrase "which promoter is induced at and/or adjacent to a target site" (reply page 16).

The rejection is maintained because the recitation of "target site" in the rejected claims remains indefinite.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 22 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 22 as amended is directed to a cell of a plant transformed with a chimaeric gene according to the method of claim 1.

Claim 22 as written does not sufficiently distinguish over plant cells as they exist naturally because the claim does not particularly point out that the cell is a non-naturally occurring product. While the claim requires that the cell be "of a plant transformed with a chimaeric gene according to the method of claim 1", the claim does not require that the cell itself comprise the chimaeric gene. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claim should be amended to indicate the hand of the inventor, e.g., by indicating that the cell comprises the chimaeric gene used to transform the plant from which the cell was obtained.

Claim Rejections - 35 USC § 102

Claims 1, 7, 10, 11-17, 21-23 and 26 remain rejected under 35 U.S.C. 102(b) as being anticipated by Maddaloni et al. (Transgenic Research, 1997, Vol. 6, No. 6, pages 393-402), for the reasons of record set forth in the office action mailed December 24, 2003.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

Applicant requests withdrawal of the rejection of claims because Maddaloni et al. do not disclose each and every element of the present invention. Applicant points out that the method disclosed in Maddaloni et al. directs the ribosome inactivating protein against an invading external eukaryote *Rhizoctonia solani*, and that in contrast to the constitutive promoter used by Maddaloni et al., the present invention involves a target tissue specific inducible promoter linked to a coding sequence, the expression of which causes plant cytotoxicity of the host plant at a target site when the promoter is induced at and/or adjacent to the target site. (reply page 18)

The rejection is maintained because Maddaloni et al. disclose each and every element of the claimed invention. In response to Applicant's argument that Maddaloni et al. fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., "target tissue specific inducible promoter" and presumably a corresponding plant target tissue) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The rejected claims encompass the use of any unspecified promoter which is induced at and/or adjacent to any unspecified target site. Accordingly the rejected claims encompass the use of the potato wound-inducible wun1

promoter (a nonconstitutive promoter) as taught by Maddaloni et al., which is induced by wounding at, and or adjacent to, a wounding target site.

Claim Rejections - 35 USC § 103

Claims 1, 3 and 14-17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Maddaloni et al. (Transgenic Research, 1997, Vol. 6, No. 6, pages 393-402) in view of Hey et al. (Plant Physiology, 1995, Vol. 107, pages 1323-1332) and Boston et al. (US 5,332,808 issued July 26, 1994, Applicant's IDS), for the reasons of record set forth in the office action mailed December 24, 2003.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive.

Applicant argues that Maddaloni et al. do not disclose, teach, or suggest the use of a target tissue specific inducible promoter to achieve specific localized expression of maize type 3 ribosome inactivating protein at and/or adjacent to a target site in the host plant. Applicant further argues that Maddaloni et al. teach away from the present invention because Maddaloni et al. teach the use of a constitutive promoter to achieve generalized expression to promote an increased tolerance against infection from a soil-borne fungal pathogen by directing ribosome inactivating protein activity toward the invading pathogen. Applicant also argues that Maddaloni et al. do not teach localized promoter expression to induce cell death at and/or adjacent to target sites tailored, for example, to improve nematode resistance or effecting pollen sterility, but instead, concerned about cell death of the host plant, suggest that the use of high catalytic activity of ribosome inactivating proteins might not necessarily be the most appropriate strategy.

Applicant additionally argues that Hey at al. and Boston et al. do not make up for the deficiencies of Maddaloni et al., as neither Hey at al. nor Boston et al. disclose, teach, or suggest the use of a target tissue specific promoter to achieve specific localized expression at and/or adjacent to a target site.

The rejection is maintained because the claimed invention is obvious over the cited references. In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which applicant relies (i.e., "target tissue specific inducible promoter" and presumably a corresponding plant target tissue, and localized promoter expression to induce cell death at and/or adjacent to target sites tailored to improve nematode resistance or effecting pollen sterility) are not recited in the rejected claim(s). The rejected claims encompass producing a transgenic plant by using a chimaeric gene comprising any unspecified promoter which is induced at and/or adjacent to any unspecified target site, wherein expression of the gene causes plant cytotoxicity at a target site. Accordingly the rejected claims encompass the use of the potato wound-inducible wun1 promoter (a nonconstitutive promoter) as taught by Maddaloni et al., which is induced by wounding at, and or adjacent to, a wounding target site. Furthermore, in using a wound-inducible wun1 promoter, Maddaloni et al. do teach localized promoter expression to induce cell death at and/or adjacent a target sites.

With respect to Maddaloni et al. teachings concerning cell death of the host plant and the high catalytic activity of ribosome inactivating proteins, Maddaloni et al. teach at page 400 column 1 that the susceptibility of plant ribosomes to a ribosome inactivating protein depends on the source of both the ribosomes and the ribosome inactivating protein, with conspecific

ribosomes having at least some resistance to inactivation, such that strategies for engineering ribosome inactivating protein expression into plants need to include consideration of such specificities. Maddaloni et al. point in particular to the specific example of a pokeweed ribosome inactivating protein characterized by a high catalytic activity, which resulted in increased resistance to several viruses when expressed at a low level in transgenic plants, while high levels of expression caused severe plant deformities. Maddaloni et al. speculated that the use of high catalytic activity ribosome inactivating proteins might therefore not necessarily be the most appropriate strategy to be adopted in plant protection, and that the future efficient use of ribosome inactivating proteins in protecting plants from pathogenic organisms may reside in the fine tuning of their biological properties, such as by using a ribosome inactivating protein with a proper level of activity and a suitable promoter. Accordingly Maddaloni et al. suggest that the catalytic activity of ribosome inactivating proteins and their potential to affect the ribosomes of transgenic host plants needs to be taken into consideration when using ribosome inactivating proteins to protect plants from pathogenic organisms. In this regard it is noted that the induction of localized plant cell death could be considered a desirable phenotypic trait in response to certain plant pathogens, e.g. those that would be excluded by a hypersensitive response.

With respect to Hey at al. and Boston et al., neither reference need disclose, teach, or suggest the use of a target tissue specific promoter in order to render the claimed invention obvious, as the claimed invention does not require the use of a target tissue specific promoter. Furthermore, Hey at al. and Boston et al. were not cited for their teachings with respect to promoters. Hey et al. was cited for teaching a biologically active recombinant mature maize RIP

comprising an α domain and a β domain arranged contiguously, and Boston et al. was cited for teaching the use of a nos terminator in a plant expression construct.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600